EMA/451036/2021

European Medicines Agency decision

P/0346/2021

of 18 August 2021

on the acceptance of a modification of an agreed paediatric investigation plan for pegylated-fibroblast growth factor 21 (BMS-986036) (EMEA-002448-PIP01-18-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0336/2019 issued on 10 September 2019, and decision P/0387/2020 issued on 1 October 2020,

Having regard to the application submitted by Bristol-Myers Squibb International Corporation on 14 April 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 23 July 2021, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for pegylated-fibroblast growth factor 21 (BMS-986036), solution for injection, subcutaneous use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Bristol-Myers Squibb International Corporation, Parc de l'Alliance, Avenue de Finlande 4. 1420 - Braine-l'Alleud, Belgium.

EMA/PDCO/256617/2021 Corr
Amsterdam, 23 July 2021

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-002448-PIP01-18-M02

Scope of the application

Active substance(s):

Pegylated-fibroblast growth factor 21 (BMS-986036)

Condition(s):

Treatment of non-alcoholic steatohepatitis

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Bristol-Myers Squibb International Corporation

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bristol-Myers Squibb International Corporation submitted to the European Medicines Agency on 14 April 2021 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0336/2019 issued on 10 September 2019, and decision P/0387/2020 issued on 1 October 2020.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 25 May 2021.

Scope of the modification

Some timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of non-alcoholic steatohepatitis (NASH)

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- solution for injection, subcutaneous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s);

  and

- the paediatric population from 2 years to less than 8 years of age;
- solution for injection, subcutaneous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition:

Treatment of non-alcoholic steatohepatitis (NASH)

2.1.1. Indication(s) targeted by the PIP

Treatment of NASH with moderate to severe liver fibrosis

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 8 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an age-appropriate presentation for dose(s) with 20 mg/mL BMS-986036 in vials for use in PIP Study 8 in patients from 8 years to less than 18 years of age with NASH with moderate to severe fibrosis.

		Study 2 Development of an age-appropriate dose(s) with 20 mg/mL (or lower concentration, if needed) BMS-986036 in vials or in prefilled syringe or prefilled pen for use in PIP Study 9 and, if appropriate, for commercialisation.
Non-clinical studies	5	**Study 3** Toxicology study in pregnant and lactating Sprague-Dawley rats (aged 10 to 11 weeks at dose initiation) and the offspring. **Study 4** Four-week, exploratory, dose-range finding, and toxicity study in juvenile rats, aged 21 days through day 50. **Study 5** Ten-week, definitive, toxicology study in juvenile rats, plus a recovery period. **Study 6** Single-dose study in adult monkeys with radiolabeled BMS-986036. **Study 7** Repeat-dose study in adult monkeys with BMS-986036 to evaluate distribution of BMS-986036 and PEG into various organs at steady-state.
Clinical studies	2	**Study 8** 16-week, randomized, double-blind, placebo-controlled, parallel-group, multiple-dose study to assess the pharmacokinetics (PK), pharmacodynamics (PD), initial safety, and tolerability of BMS-986036 in children and adolescent patients from 8 years to less than 18 years of age with NASH with moderate to severe fibrosis. **Study 9** 48-week, double-blind, placebo-controlled study to assess the safety and efficacy of BMS-986036 in children and adolescent subjects from 8 years to less than 18 years of age with NASH with moderate to severe fibrosis.
Extrapolation, modelling and simulation studies	0	Not applicable
Other studies	0	Not applicable
Other measures	0	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By October 2029
Deferral for one or more measures contained in the paediatric investigation plan:	Yes